succinic semialdehyde dehydrogenase deficiency

Succinic semialdehyde dehydrogenase deficiency is a disorder that can cause a variety of neurological problems. People with this condition typically have developmental delay, especially involving speech development; intellectual disability; and decreased muscle tone (hypotonia) soon after birth. About half of those affected experience seizures, difficulty coordinating movements (ataxia), decreased reflexes (hyporeflexia), and behavioral problems. The most common behavioral problems associated with this condition are sleep disturbances, hyperactivity, difficulty maintaining attention, and anxiety. Less frequently, affected individuals may have increased aggression, hallucinations, obsessive-compulsive disorder (OCD), and self-injurious behavior, including biting and head banging. People with this condition can also have problems controlling eye movements. Less common features of succinic semialdehyde dehydrogenase deficiency include uncontrollable movements of the limbs (choreoathetosis), involuntary tensing of the muscles (dystonia), muscle twitches (myoclonus), and a progressive worsening of ataxia.

Frequency

Approximately 350 people with succinic semialdehyde dehydrogenase deficiency have been reported worldwide.

Genetic Changes

Mutations in the *ALDH5A1* gene cause succinic semialdehyde dehydrogenase deficiency. The *ALDH5A1* gene provides instructions for producing the succinic semialdehyde dehydrogenase enzyme. This enzyme is involved in the breakdown of a chemical that transmits signals in the brain (neurotransmitter) called gamma-amino butyric acid (GABA). The primary role of GABA is to prevent the brain from being overloaded with too many signals.

A shortage (deficiency) of succinic semialdehyde dehydrogenase leads to an increase in the amount of GABA and a related molecule called gamma-hydroxybutyrate (GHB) in the body, particularly the brain and spinal cord (central nervous system). It is unclear how an increase in GABA and GHB causes developmental delay, seizures, and other signs and symptoms of succinic semialdehyde dehydrogenase deficiency.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal

recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- 4-hydroxybutyric aciduria
- 4-hydroxybutyricaciduria
- Gamma-hydroxybutyric acidemia
- gamma-hydroxybutyric aciduria
- SSADH deficiency

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Succinate-semialdehyde dehydrogenase deficiency
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268631/

Other Diagnosis and Management Resources

- GeneReview: Succinic Semialdehyde Dehydrogenase Deficiency
  https://www.ncbi.nlm.nih.gov/books/NBK1195
- MedlinePlus Encyclopedia: Hyperactivity
  https://medlineplus.gov/ency/article/003256.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Hyperactivity
  https://medlineplus.gov/ency/article/003256.htm
- Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html
- Health Topic: Movement Disorders
  https://medlineplus.gov/movementdisorders.html
- Health Topic: Seizures
  https://medlineplus.gov/seizures.html
- Health Topic: Speech and Communication Disorders
  https://medlineplus.gov/speechandcommunicationdisorders.html

Genetic and Rare Diseases Information Center

- Succinic semialdehyde dehydrogenase deficiency
  https://rarediseases.info.nih.gov/diseases/7695/succinic-semialdehyde-dehydrogenase-deficiency

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Epilepsy Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Epilepsy-Information-Page

Educational Resources

- Boston Children's Hospital: Seizures and Epilepsy
  http://www.childrenshospital.org/conditions-and-treatments/conditions/seizures
- Disease InfoSearch: Succinic semialdehyde dehydrogenase deficiency
  http://www.diseaseinfosearch.org/Succinic+semialdehyde+dehydrogenase+deficiency/6917
- MalaCards: succinic semialdehyde dehydrogenase deficiency
  http://www.malacards.org/card/succinic_semialdehyde_dehydrogenase_deficiency
- Merck Manual Home Edition for Patients and Caregivers
  http://www.merckmanuals.com/home/brain-spinal-cord-and-nerve-disorders/seizure-disorders/seizure-disorders
- Orphanet: Succinic semialdehyde dehydrogenase deficiency
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=22

Patient Support and Advocacy Resources

- American Epilepsy Society
  https://www.aesnet.org/
- CLIMB: Children Living with Inherited Metabolic Diseases
  http://www.climb.org.uk/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/succinic-semialdehyde-dehydrogenase-deficiency/
- Pediatric Neurotransmitter Disease Association
  http://www.ssadh.net/site/c.ahJMLVMwGcK0E/b.8193573/k.E42C/SSADH__Succinic_Semialdehyde_Dehydrogenase_Deficiency.htm

GeneReviews

- Succinic Semialdehyde Dehydrogenase Deficiency
  https://www.ncbi.nlm.nih.gov/books/NBK1195

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22succinic+semialdehyde+dehydrogenase+deficiency%22+OR+%22brain+diseases%2C+metabolic%2C+inborn%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28succinic+semialdehyde+dehydrogenase+deficiency%5BTIAB%5D%29+OR+%284-hydroxybutyric+aciduria%5BTIAB%5D%29+OR+%28gamma-hydroxybutyric+aciduria%5BTIAB%5D%29%29+OR+%28SSADH+deficiency%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- SUCCINIC SEMIALDEHYDE DEHYDROGENASE DEFICIENCY
  http://omim.org/entry/271980

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